UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/626,053	07/24/2003	Claus Yding Andersen	6203.214-US	1429

7590 04/23/2007

Reza Green
Novo Nordisk Pharmaceuticals, Inc.
100 College Road West
Princeton, NJ 08540

EXAMINER	
SAUCIER, SANDRA E	
ART UNIT	**PAPER NUMBER**
1651	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/626,053	ANDERSEN ET AL.	
	Examiner	Art Unit	
	Sandra Saucier	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19,21,23-25,27,42 and 43* is/are pending in the application.

4a) Of the above claim(s) *25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19,21,23,24,27,42 and 43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/23/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 19, 21, 23-25 27, 42, 43 are pending. Claims 19, 21, 23, 24, 27, 42 and 43 are considered on the merits. Claim 25 is withdrawn from consideration as being drawn to a non-elected invention.

Election/Restriction

Applicants species election of FF-MAS for examination is acknowledged.

Claim Rejections - 35 USC § 112

INDEFINITE

Claims 19, 21, 23, 24, 27, 42 and 43 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Please do not use abbreviations in the claims at least without prior definition in the claims.

Claim 19 still uses MAS which is not defined.

Claim 21 uses M11 which is not defined.

Claim 43 uses 'Mil" which is not defined.

Please observe that the abbreviations for metaphase II are not consistent throughout the claims.

Claim Rejections - 35 USC § 102

Claims 19, 21, 23, 24, 42 and 43 remain rejected under 35 U.S.C. 102(b) as being clearly anticipated by US 5,716,777 [A] or WO 96/00235 [N] in light of Smitz *et al.* [U].

The claims are directed to a method for *in vitro* fertilization comprising: culturing oocytes in metaphase II with spermatozoa in a culture medium which comprises MAS, thereby
forming zygotes or pre-embryos.

The elected species is FF-MAS which is 4,4-dimethyl-5α-cholesta-8,14,24-triene-3β-ol.

The references are relied upon as explained below.

US 5,716,777 or WO 96/00235 contain essentially the same material. The references disclose that "when *in vitro* fertilization is performed, better results are achieved, when a meiosis inducing substance of formula (I) is added to the medium in which the oocytes are kept." The compounds of formula (I), include 4,4-dimethyl-5α-cholesta-8,14,24-triene-3β-ol, col. 5. Please note that in Example 10, the mice were given a gonadotropin injection and allowed to wait 48 hours before oocyte collection. Thus, the oocytes are not homogeneous with regard to the phase of maturation and the population should have oocytes in MII due to the gonadotropin regime.

Smitz *et al.* is a review which demonstrates what is known in the art of *in vitro* fertilization. It shows schematically in Figure 1, the different techniques to culture oocytes in relation to the stage of development of the oocyte. The culturing of oocyte-cumulus complex as well as of a denuded oocyte is demonstrated. After ovulation induction for IVF (gonadotropin administration), 80% of the harvested oocytes are metaphase II and the remaining oocytes are either metaphase I or GV (page 150). Therefore incubation of these oocytes, as is routine in the art, would include metaphase I, metaphase II and GV oocytes. Routinely, for *in vitro* fertilization, spermatozoa are added to the medium and oocytes allowed to be fertilized and divide, prior to selection of a few blastocysts or embryos for implantation.

Thus, the teaching of US 6,716,777 or WO 96/00235 of the addition of a meiosis-stimulating sterol to the incubation medium of the oocyte in a method of *in vitro* fertilization, inherently incorporates all the steps routine in *in vitro* fertilization methods.

Claim Rejections - 35 USC § 103

Claims 19, 21, 23, 24, 27, 42 and 43 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Smitz *et al.* [U] or US 5,693,534 [B] in combination with US 5,716,777 [A] or WO 96/00235 [N].

The claims have been discussed above.

Smitz et al. disclose that in routine IVF procedures, after routine gonadotropin administration schedule, harvested oocytes are 80% in MII. When cultured in standard IVF medium, further maturation of the immature oocytes which were collected to MII is obtained (page 150). In Figure 1, in vitro maturation of antral, preovulatory oocytes is shown. The inference to be drawn from this statement is that 20% of the oocytes are in earlier stages than MII. The reference lacks the inclusion of the claim specific sterol in the incubation medium.

US 5,716,777 and WO 96/00235 were explained above.

US 5,693,534 is cited to show what is known and routine in the art of IVF (cols. 5 and 6). At col. 5, l. 62, it is stated that after gonadotropin administration *in vivo* to induce maturation of oocytes, about 40% of the oocytes are already at MII at time of collection. In the examples, immature oocytes from an unstimulated animal (no gonadotropin administrations) are cultured and develop into MII oocytes

Smitz *et al.* and US 5,693,534 lack the inclusion of a sterol in the medium used for oocyte maturation and fertilization.

The addition of a meiosis stimulating sterol such as FF-MAS to the culture medium of oocytes used in IVF in the method of Smitz et al. would have been obvious when taken with US 5,716,777 or WO 96/00235 because both suggest such an addition.

One of ordinary skill in the art would have been motivated at the time of invention to make this addition in order to obtain the results as suggested by the references with a reasonable expectation of success. The claimed subject matter fails to patentably distinguish over the state of the art as represented by the cited references. Therefore, the claims are properly rejected under 35 U.S.C. § 103.

Response to Arguments

Applicants' arguments filed 2/12/07 have been fully considered but they are not persuasive.

Applicants argue that US 5,716,777 relates to the resumption of meiosis in oocytes from the prophase of the first meiotic division (meiosis I) using MAS. However, a careful reading of the document does not support this narrower finding urged by applicants. Please see col. 3, l. 39, where it is stated "Also, when in vitro fertilization is performed, better results are achieved, when a meiosis inducing substances of formula (I) is added to the medium in which the oocytes are kept.". Thus, it is difficult to find support in US 5,716,777 for applicant's urging, particularly with regard to the blanket statement concerning the utility of the instant sterols in *in vitro* fertilization techniques which include according to Smitz et al. harvesting oocytes after induction by gonadotropin treatment and that harvested oocytes in routine IVF procedures are a mixture of stages of oocytes, some of which are MII phase oocytes. Applicants point to the section of US '777 where it is stated that "For use as a contraceptive agent in females, a meiosis inducing substance can be administered so as to prematurely induce resumption of meiosis in oocytes while they are still in the growing follicle, before the ovulatory peak of gonadotropins occurs." to support their contention that US '777 discloses solely MI to MII maturation. However,

the cited passage is not directed to IVF procedures and the patent is silent with regard to the phase of maturation of the oocytes, which would be a mixture of maturation phases according to Smitz et al. when harvested according to routine IVF methods. Thus, the suggestion of US '777 to include a MAS in the culture medium with the oocytes harvested for an IVF method after routine administration of gonadotropins and which incorporates the addition of spermatozoa, see Smitz et al. for routine procedures, would inherently have oocytes in MII, in the culture medium with the spermatozoa. Applicants argue that the addition of MAS would be beneficial in respect of formation of zygotes. There is no evidence presented in the application showing higher implantation rates upon incubation in a culture medium which contains a MAS. The exemplification is to culturing oocytes in the presence of added FSH and EGF. This is not the same as and is not a direct showing of the addition of a MAS to MII oocytes and an increase in implantation rates. Thus, there are no unexpected results in the specification which are commensurate in scope with the claim method.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Applicant should specifically point out the support for any amendments made to the disclosure, including the claims (MPEP 714.02 and 2163.06). Due to the procedure outlined in MPEP 2163.06 for interpreting claims, it is noted

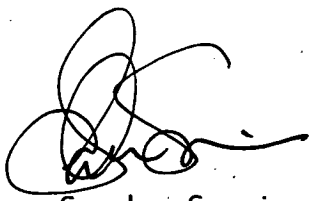
that other art may be applicable under 35 USC 102 or 35 USC 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to the office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Saucier whose telephone number is (571) 272-0922. The examiner can normally be reached on Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, M. Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Sandra Saucier
Primary Examiner
Art Unit 1651
April 17, 2007